

Figure 1

15.5      11



Figure 2

1 SAIKGRFELQILRMLIVDROGCTPMLLGSVFTIHRQELITLTICLIFESSYFVLAEDAVNEGRVEFGSYADALWAWVTTTIGDRYVPTOWVCKTIA  
   :|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:  
   ATLRLVLLDVRVRAEFLXSLRSLKQIQLQRTLXASRRELQFLAEEFLGOMLESSAYFREAGERSRF...FKSIPDLMWAWVTTTIGDRYVPTOWVCKTIA  
 2 81. 82. 83. 84. 85. 86. 87. 88. 89. 90. 91. 92. 93. 94. 95. 96.

Figure 3

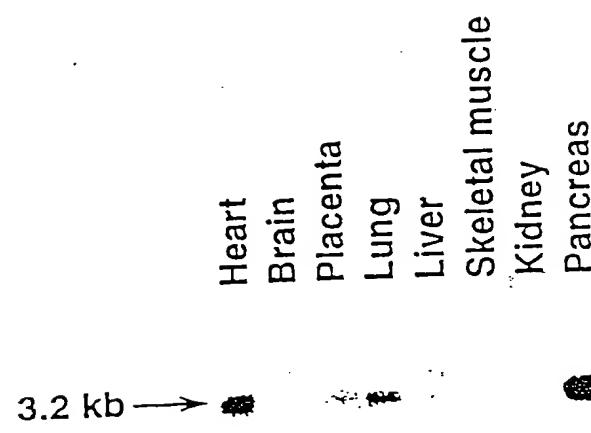


Figure 4

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 ATGGCCGCGGCCCTCCCTCCCCGCCAGGGCGAGAGGAAGCGCTGGGGCTGGCCAGGCCCTCGCTACCGCCTCGTT-243  
 M A A A S S P P R A E R K R W G W G R L P G A R R G S -27  
 GCGGCCCTGGCCAAGAAGTGCCTCTCGCTGGAGCTGGCCGGAGGGCGCCGGCGGGCGCCTACCGCCTCGATCGCCTCGATC-324  
 A G L A K K C P F S L E L A E E G G P A G G A L Y A P I -54  
 GCGCCCGGCCAGGTCCCAGGCCCTCGCTCCCCGGCCGCCGGCCGGCCAGTTGCCTCCGACCTTGCCCG-405  
 A P G A P G P A P P A S P A A P A P P V A S D L G P -81  
 CGGCCGCCGGTGAGCCTAGACCCGCGCTCTACAGCACGCGCCGGTGTGGCGCGCACCGTCCAGGGC-486  
 R P P V S L D P R V S I Y S T R R P V L A R T H V Q G -108  
 ▼  
 CGCGTCTACAACCTCCTCGAGCGTCCCACCGGCTGGAAATGCTTCGTTACCACTTCGCCGCTTCCTCATCGTCCGGTC-567  
 R V Y N F L E R P T G W K C F V Y H F A V F L I V L V -135  
 ▼ S1  
 TGCCTCATCTTCAGCGTGTGTCACCATCGAGCACTATGCCGCCCTGGCCACGGGACTCTCTCTGGATGGAGATCGTG-648  
 C L I F S V L S T I E Q Y A A L A T G T L F W M E I V -162  
 S2  
 CTGGTGGTGTCTTCGGGACGGAGTACGTGGTCCGCCCTCGTCCGCCAGCAAGTACGTGGGCTCTGGGG-729  
 L V V F E G T E Y V V R L W S A G C R S K Y V G L W G -189  
 ▼  
 CGGCTGCCTTGCCCCGAAGCCCATTCCATCATCGACCTCATCGTGGTGTGGCCCTCATGGTGGTCTCTGGTGGG-810  
 R L R F A R K P I S I I D L I V V V A S M V V L C V G -216  
 S3  
 TCCAAGGGGCAGGTGTTGCCACGTCGGCATCGGGCATCCGCTCTGCAGATCCTGAGGATGCTACACGTCGACCCG-891  
 S K G Q V F A T S A I R G I R F L O I L R M L H V D R -243  
 S4  
 CAGGGAGGCACCTGGAGGCTCCGGCTCCGGTGTCTCATCCACCGCAGGAGCTGATAACCACCTGTACATCGGCTTC-972  
 Q R G G T W R L L G S V V F I H R Q E L I T T L Y I G F -270  
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 L I G L I F S S Y F V Y L A E K D A V N E S G R V E F G -297  
 S5  
 AGCTACGCAGATCGCCTGGTGGGGGGTGTACAGTCACCAACATCGGCTATGGGACAAGGTGCCCCAGACGTGGTC-1134  
 S W Y A D A L W W G V V T V T I G Y G D K V P Q T W V -324  
 Pore  
 ▼  
 GGGAAAGACCATGCCCTCTGCTCTGTCTTGCCATCTCCCTTGCCTCCAGCGGGGATTCTGGCTCGGGTT-1215  
 G R K T I A S C F S V F A I S F F A L P A G I L G S G F -351  
 S6  
 GCCCTGAAGGTGCAGCAGAACAGAGGAGAACAGCACTTCACCGCAGATCCGGCCAGCCTCACTCATTAGACCGCA-1296  
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 W D R C Y A A E N P D S S T W K I Y I R K A P R S H T L -405  
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 L S P S P K P K K S V V V K K K F K L D K D N G V T -432  
 CCTGGAGAGAAGATGCTCACAGTCCCCATATCACGTGCAGCCCCAGAACAGAGCGGGCTGGACCACTCTCTGTCGA-1539  
 P G E K M L T V P H I T C D P P E E R R L D H F S V D -459  
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 G Y D S S V R K S P T L L E V S M P H F M R T N S F A -486  
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 GAGGACCTGGACCTGGAAGGGAGACTCTGCTGACACCCATCACCCACATCTCACAGCTGCCAACACCACCGGCCACC-1701  
 E D L D L E G E T L L T P I T H I S Q L R E H H R A T -513  
 ▼  
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 I K V I R R M Q Y F V A K K K F Q Q A R K P Y D V R D -540  
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 GTCATTGAGCAGTACTCGCAGGGCCACCTCAACCTCATGGTGCCTACAGGAGCTGCAGAGGAGGCTGGACCAAGTCCATT-1863  
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Figure 5A

```

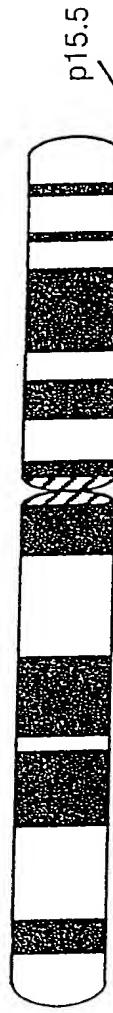
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G K P S L F I S V S E K S R D R G S N T I G A R L N R -594
    ▼

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V E D K V T Q L D Q R L A L I T D M L H Q L L S L H G -621
GGCAGCACCCCCGGCAGCGGGGCCCCCAGAGAGGGGGCCACATCACCCAGGCCAGTGGCCAGTGGCCCTCCGTC-2106
G S T P G S G P P R E G G A H I T Q P C G S G G S V -648
GACCCCTGAGCTCTTCCCTGCCAGCAACACCCCTGCCACCTACGGAGCAGCTGACCGTGCCCCAGGAGGGGGCCGATGAGGGG-2187
D P E L F L P S N T L P T Y E Q L T V P R R G P D E G -675
TCCTGAGGAGGGATGGGGCTGGGGATGGGCTGAGTGAGAGGGGAGGCCAAGAGTGCCCCACCTGGCCCTCTGAAG-2266
S * -676
GAGGCCACCTCTAAAAGGCCAGAGAGAAGAGCCCCACTCTCAGAGGCCCAATACCCCATGGACCATGCTGCTGGCAC-2349
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AGCCCTGGCCCCACATGGTGTGACATCAGGCACTGGCTGGGGGACCCAGTGGCAGGGCACAGGGCCTGGCCC-2511
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CTTGCCTGAGCTGCTGAGCGAGAGAAGTGACGGTCTTACACAGGACAGGGGCTCTGCCCCATTACATGCAAGAA-3078
ATCAATAATTGTGGTGTGATTGGATCTGTGTTAATGAGTTCACAGTGTGATTGATTAAATTGTGCAAGCTTTC-3159
CTAATAAACGTGGAGAACAC (A)n -3180

```

Figure 5B

chromosome 11



~400 kb

118A10 42B12 19D7 49E5

18B12 112E3 46F10

cos1

1 2 3 4 5 6 7 8 9 10  
11 12 13 14 15 16

KVLTQ1 exons

genomic clones

Figure 6

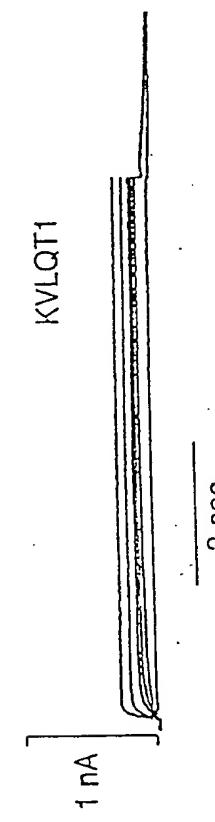
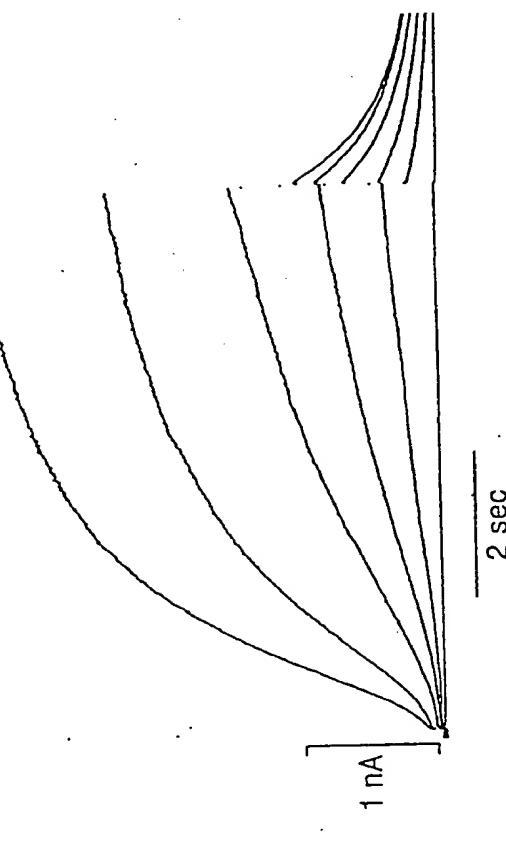
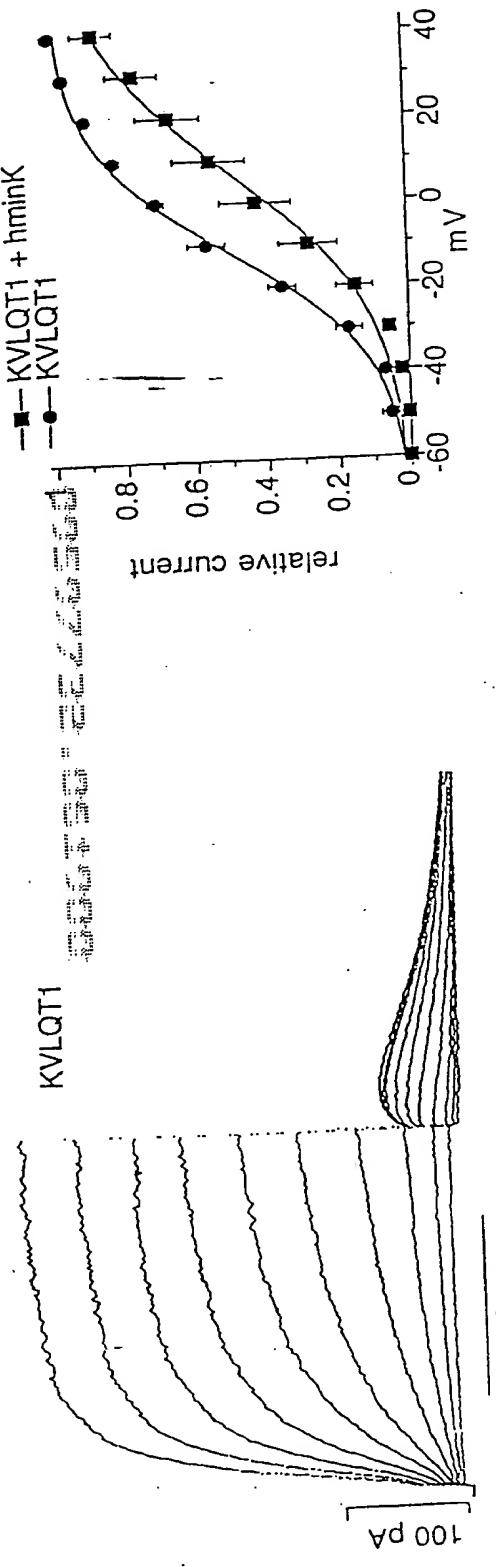


Figure 7E

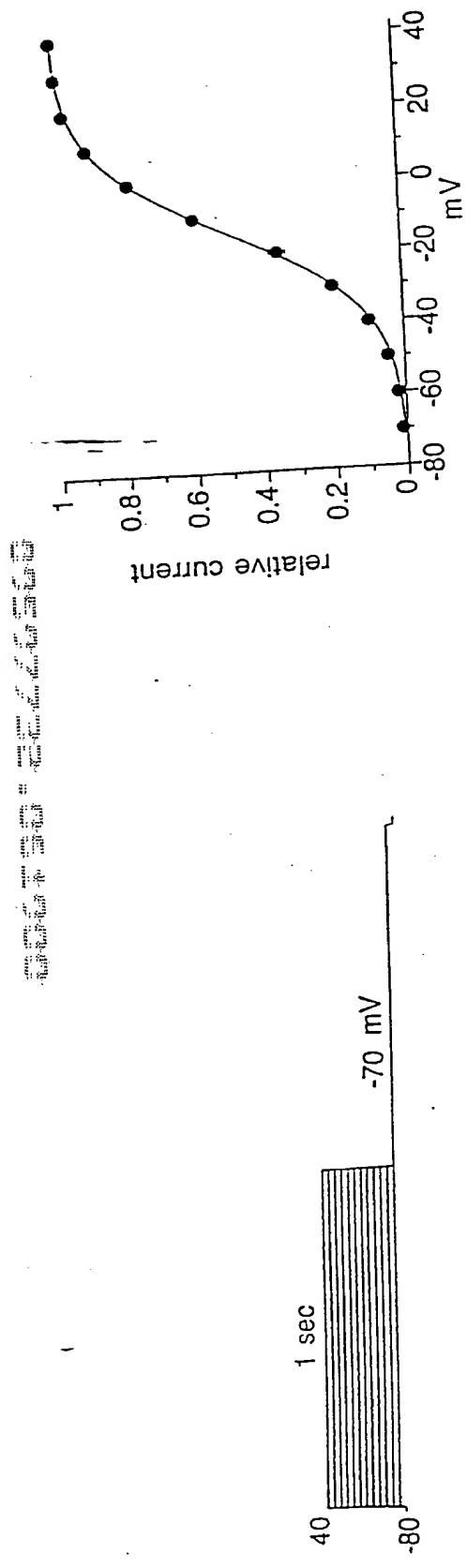


Figure 8A

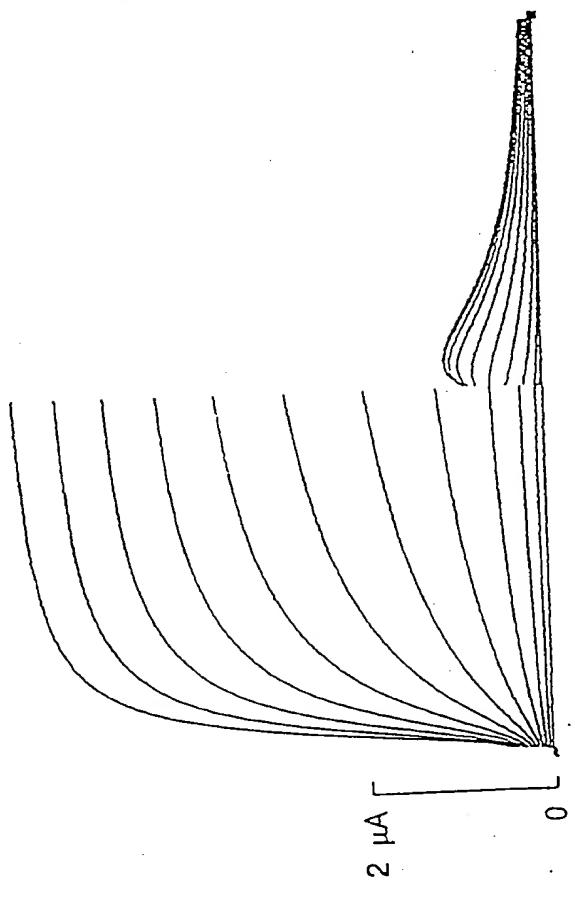


Figure 8B

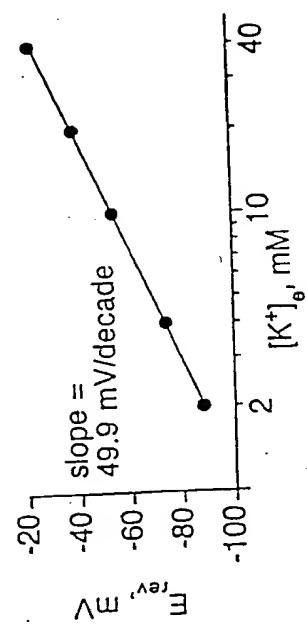


Figure 8C

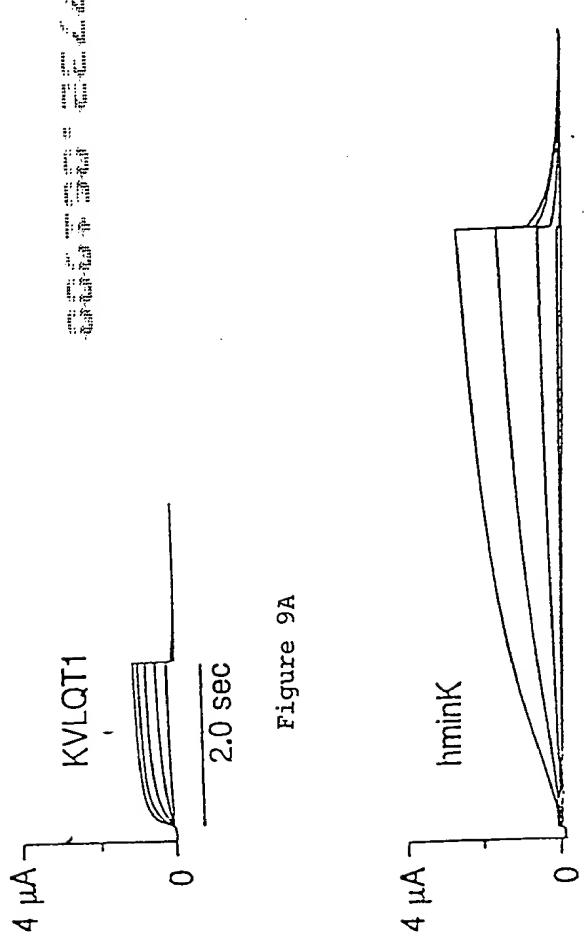


Figure 9A: Electrophysiological traces showing current responses to voltage steps. The top panel shows current traces for KVLQT1 alone (black), KVLQT1 + hminK (1 ng) (grey), and KVLQT1 + hminK (60 pg) (white). The bottom panel shows current traces for KVLQT1 alone (black) and KVLQT1 + hminK (1 ng) (grey). Scale bars: 4  $\mu$ A, 2.0 sec.

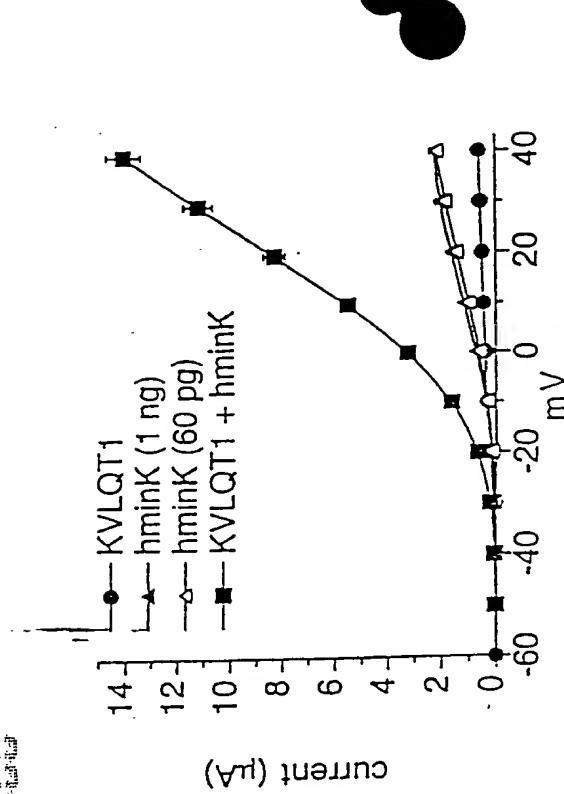


Figure 9B

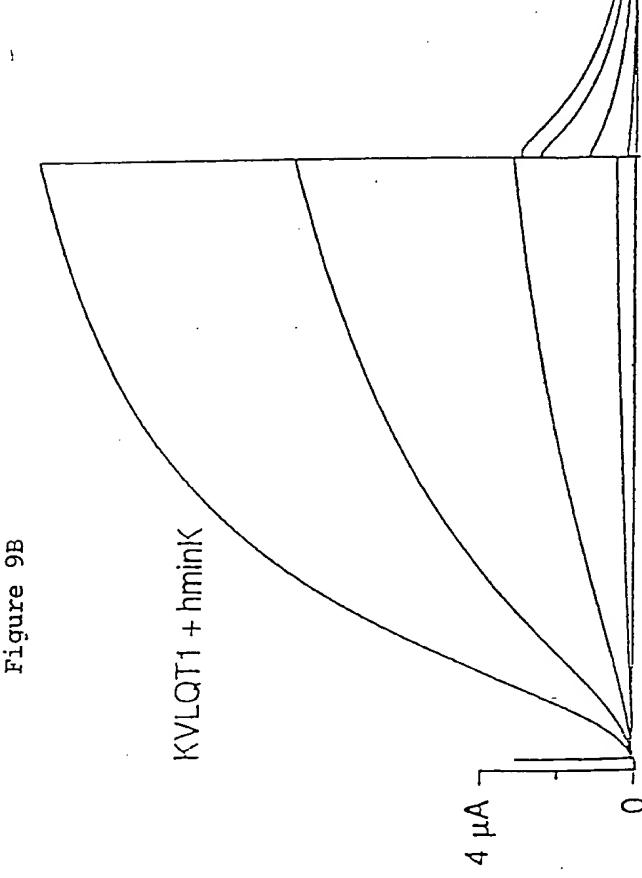


Figure 9C

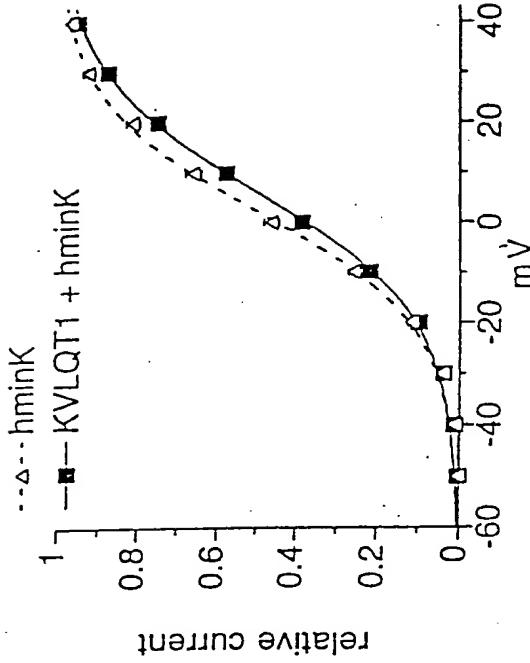


Figure 9D



Figure 9E

Xenopus	MNENAINSLYEAIPLPQDGSSNGQRQEDRQANSFELKRETIVATDPPRPT
Human	QGRVYNFLERPTGWKCFVYHFAVFLIVL
Xenopus	INLDPRVSIYSGRRPLFSRTNIQGRVYNFLERPTGWKCFVYHFTVFLIVL
Human	S1 _____ S2 _____
Xenopus	ICLIFSVLSTIQQYNNLATETLFWMEIVLVVFFGAEYVVRILSAGCRSKY
Human	VCLIFSVLSTIQQYAAALATGTLFWMEIVLVVFFGTAEYVVRILSAGCRSKY
Xenopus	VGLWGRRLRFARKPISIDLIVVVASMVLCVGSKGQVFATSAIRGIRFLQ
Human	VGVWGRRLRFARKPISIDLIVVVASVIVLCVGSNGQVFATSAIRGIRFLQ
Xenopus	S3 _____ S4 _____
Human	ILRMLHVDRQGGTWRLLGSVVFIRHQELITLTYIGFLGLIFSSYFVYLAE
Xenopus	ILRMLHVDRQGGTWRLLGSVVFIRHQELITLTYIGFLGLIFSSYFVYLAE
Human	Pore
Xenopus	KDAVNESGRVERGSYADALWWGVVTITIGYGDVKPQTWVGKTIASCFSV
Human	FAISFFALPAGILGSGFALKVQQKOROKHFNQRQIPAAASLITQTAWRACYAA
Xenopus	FAISFFALPAGILGSGFALKVQQKOROKHFNQRQIPAAASLITQTAWRACYAA
Human	ENPDSSTIWKIYIRKAPRSHILLSPSPKPKKSVVVKKKFKLKDNGVTPG
Xenopus	ENPDSATWKIYIRKQSRNHHIMSPSP
Human	EKMLTVPHITCDPPEERRLDHFSVDGYDSSVRKSPILLEVSMPHFMRTNS
Human	FAEDLDLEGETLLTPITHISQLREHHRATIKVIRRMQYFVAKKKFQQARK
Human	PYDVRDVIEQYSQGHLNLMRVIKELQRRLDQSIGKPSLFISVSEKSKDORG
Human	SNTIGARLNRVEDKVTQLDQRLALITDMLHQLLSLHGGSTPGSGGPPREG
Human	GAHITQPCGSGGSVDPELFLPSNTLPTYEQLTVPRRGPDDEGS

Figure 10

K1532

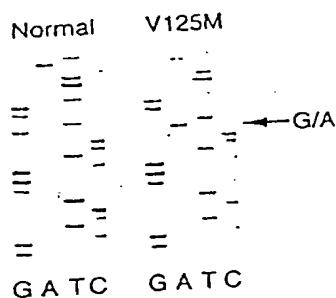
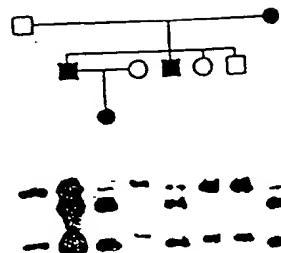


Figure 11A

K2605

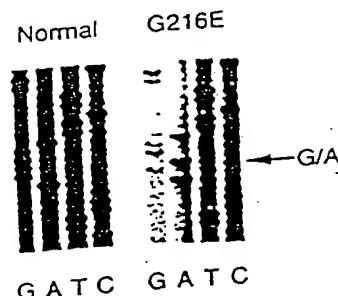
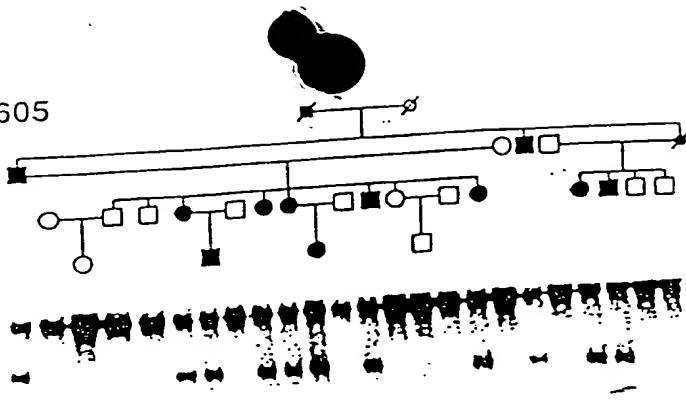


Figure 11B

K1723

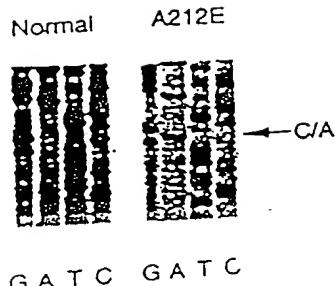
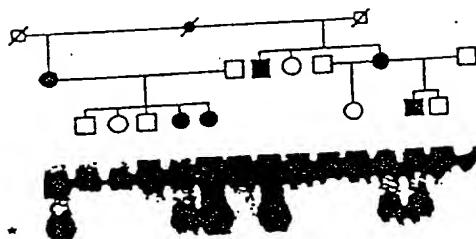


Figure 11C

K1807

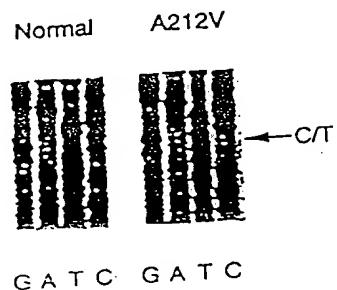
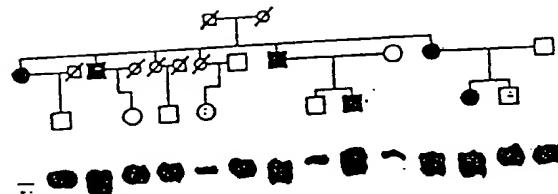
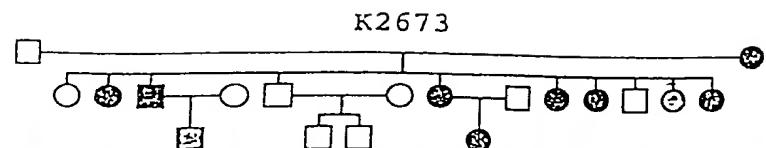
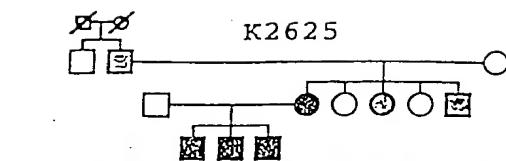


Figure 11D





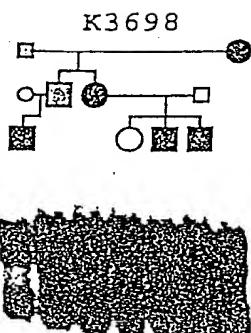
Gly168Arg

Figure 12H



Gly168Arg

Figure 12I



Gly168Arg

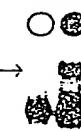
Arg366Trp

K19187



Gly314Ser

K22709



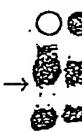
Tyr315Cys

K2762



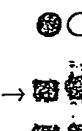
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K3401



Leu353Pro

K2824



Arg366Trp

Figure 12J

Figure 12K

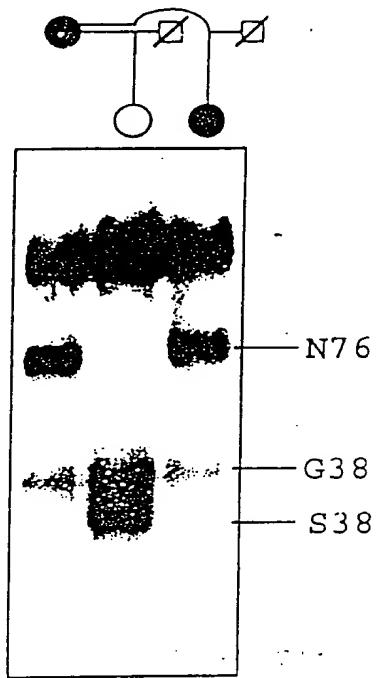
Figure 12L

Figure 12M

Figure 12N

Figure 12O

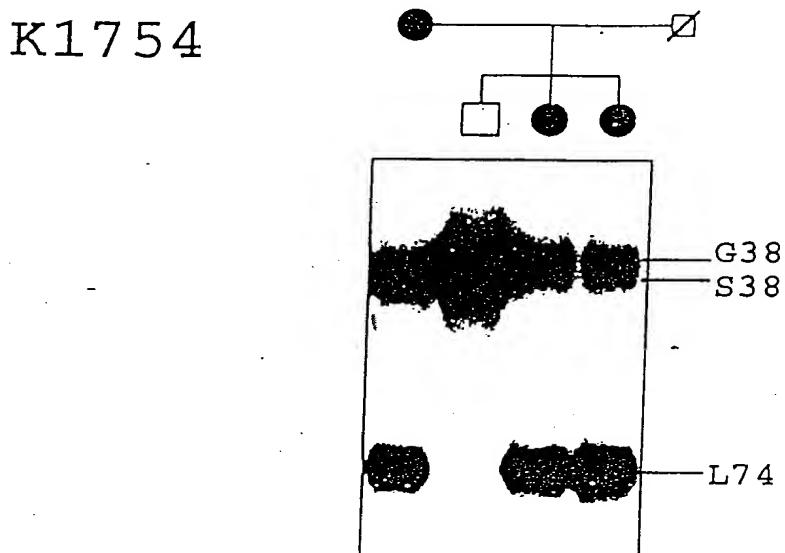
K1789



Normal	CAC	TCG	AAC	GAC	CCA	TTC	AAC
	H	S	N	D	P	F	N
↓							
Mutant	CAC	TCG	AAC	AAC	CCA	TTC	AAC
	H	S	N	N	P	F	N

Figure 13A

K1754



Normal	CTG	GAG	CAC	TCG	AAC	GAC	CCA
	L	E	H	S	N	D	P
↓							
Mutant	CTG	GAG	CAC	TTG	AAC	GAC	CCA
	L	E	H	L	N	D	P

Figure 13B

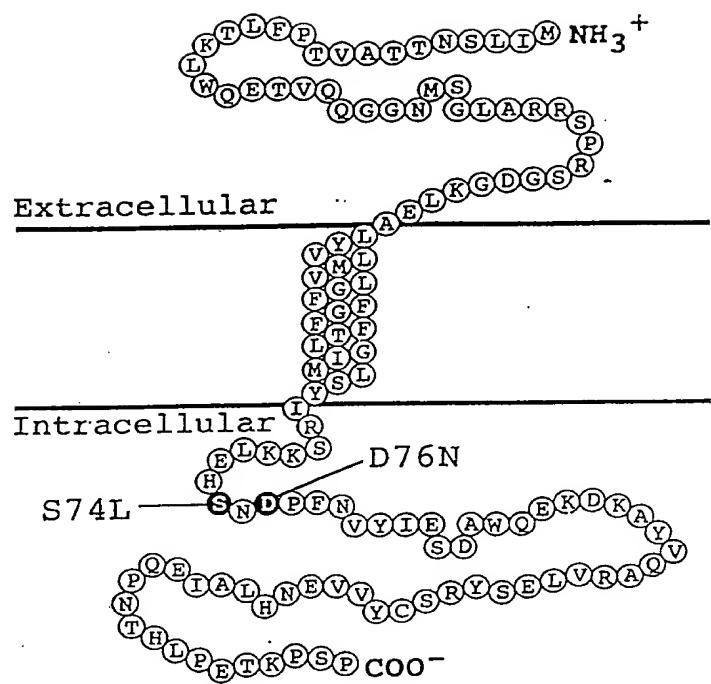


Figure 13C

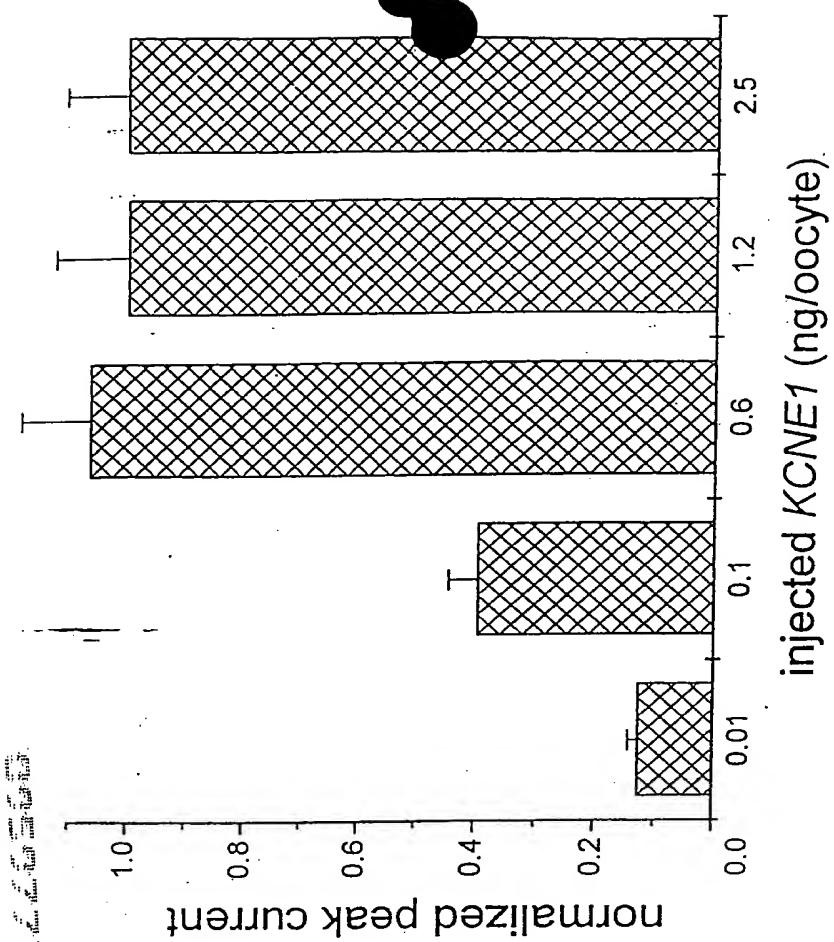


Figure 14B

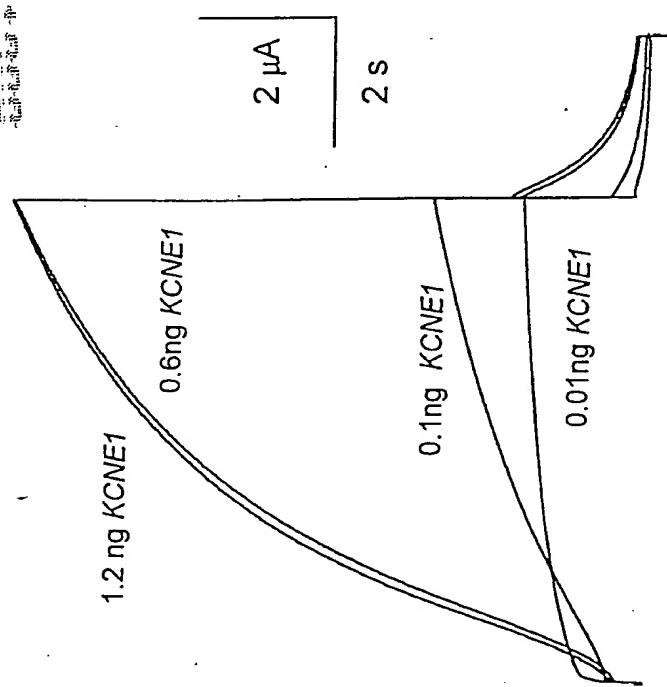


Figure 14A

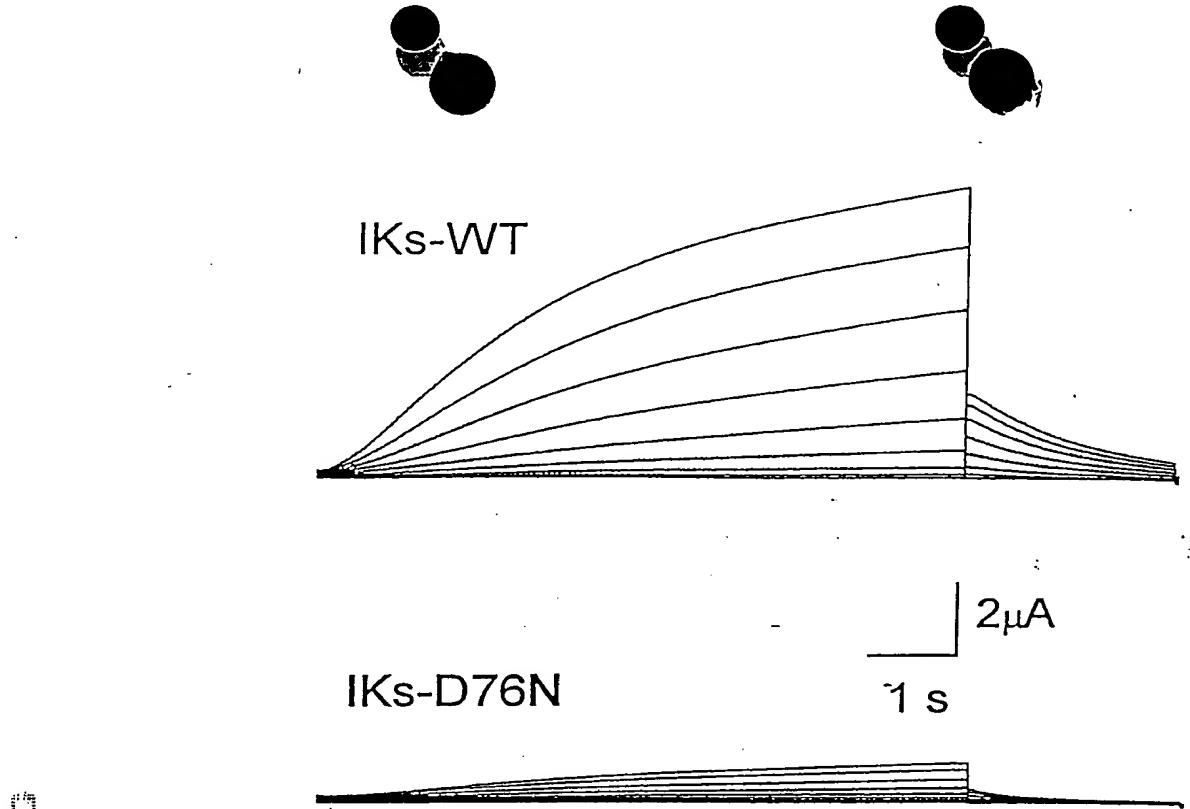


Figure 15A

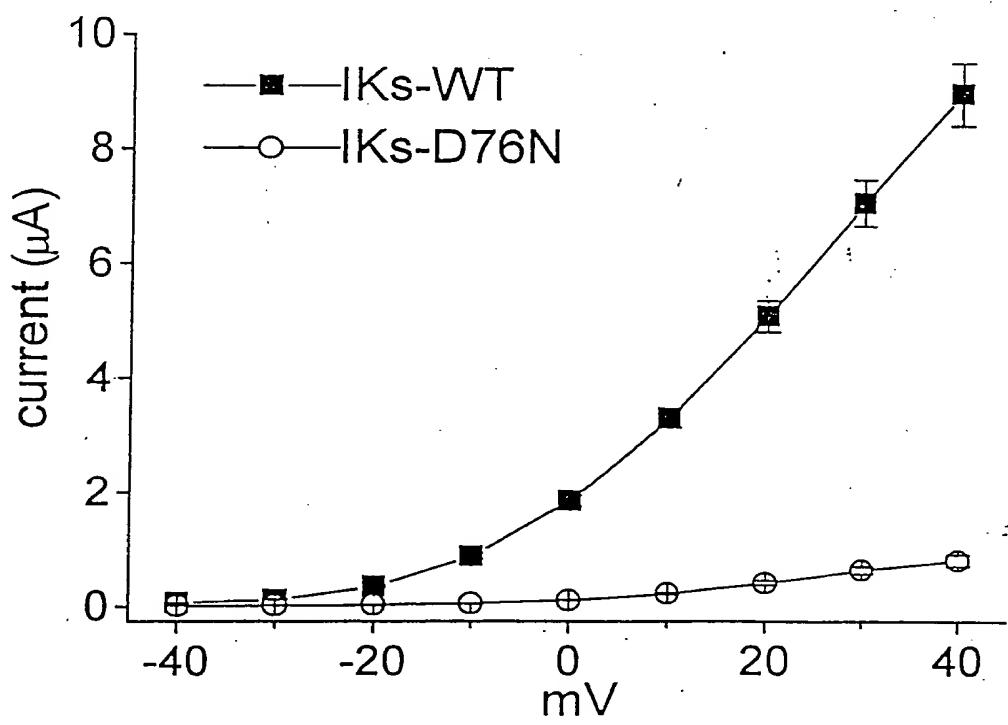


Figure 15B

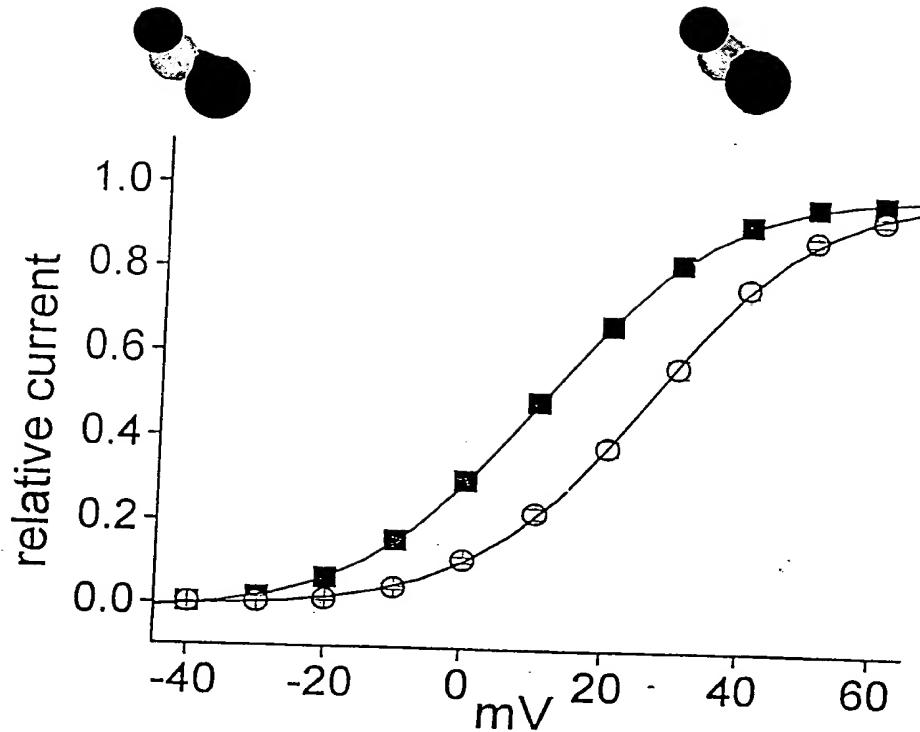


Figure 15C

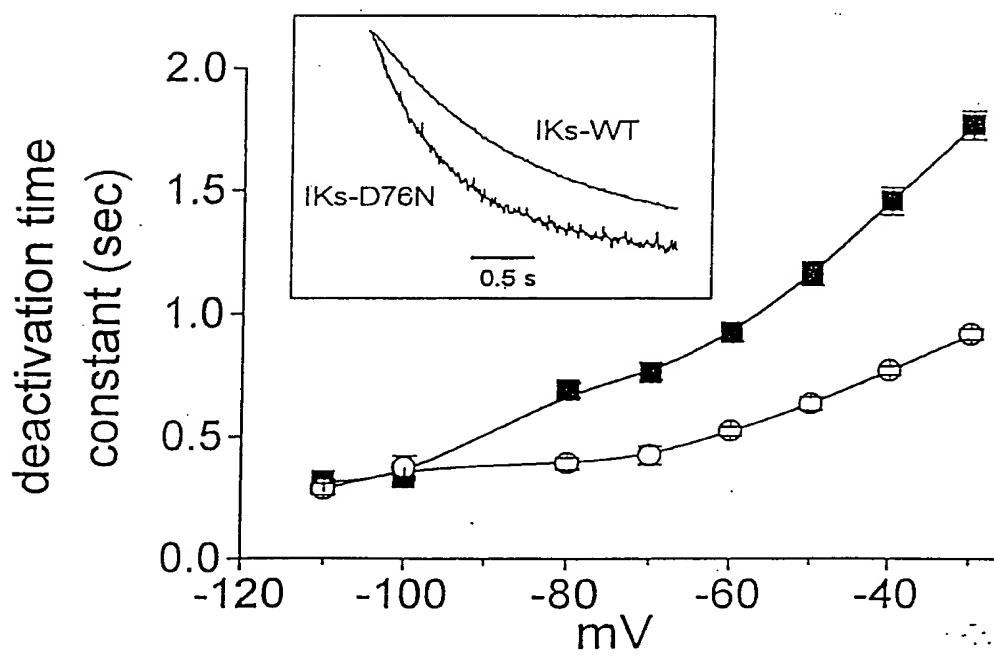


Figure 15D

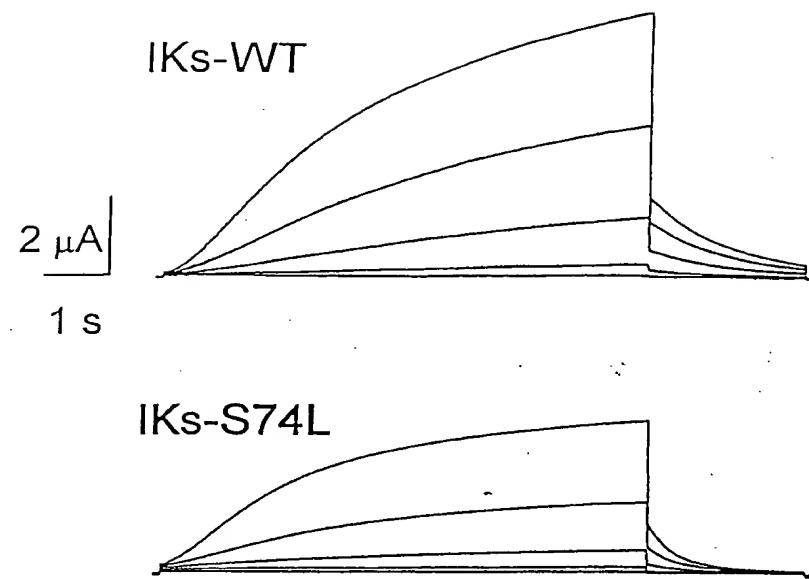


Figure 16A

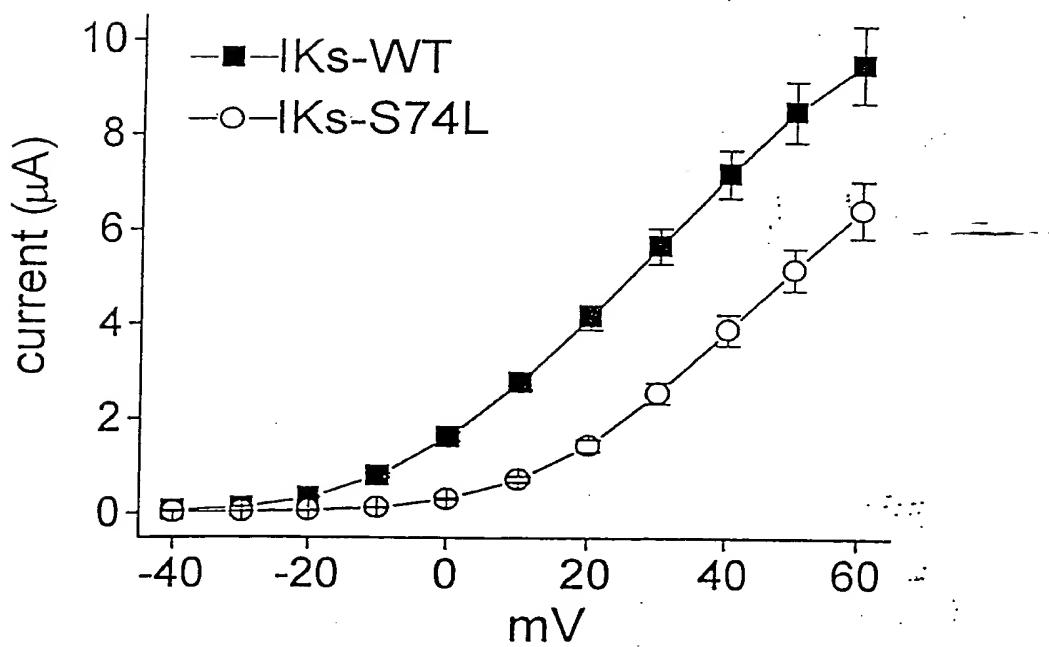


Figure 16B

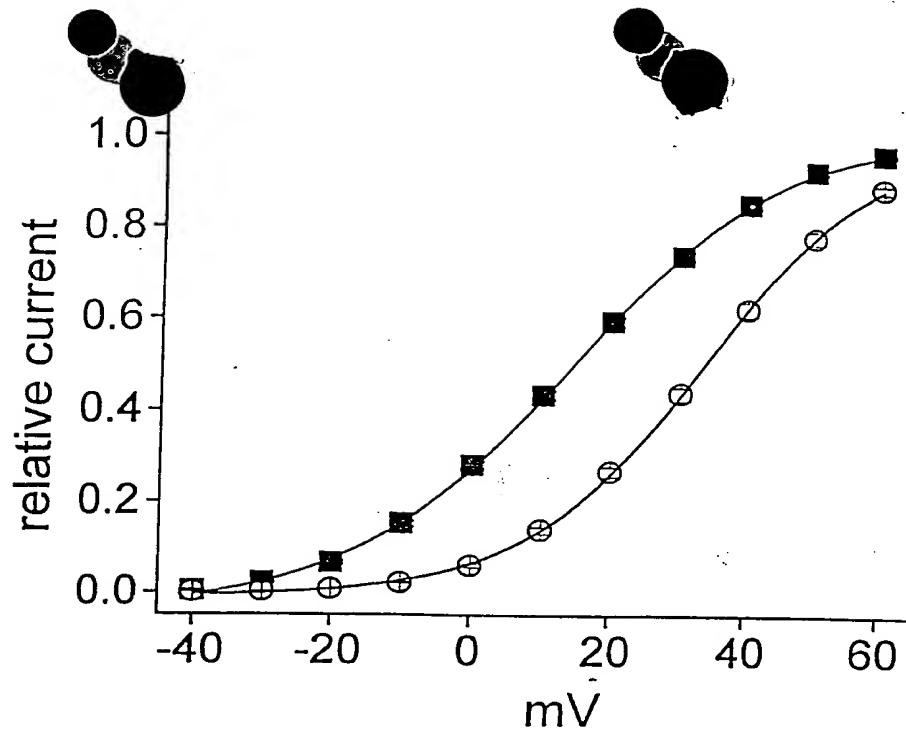


Figure 16C

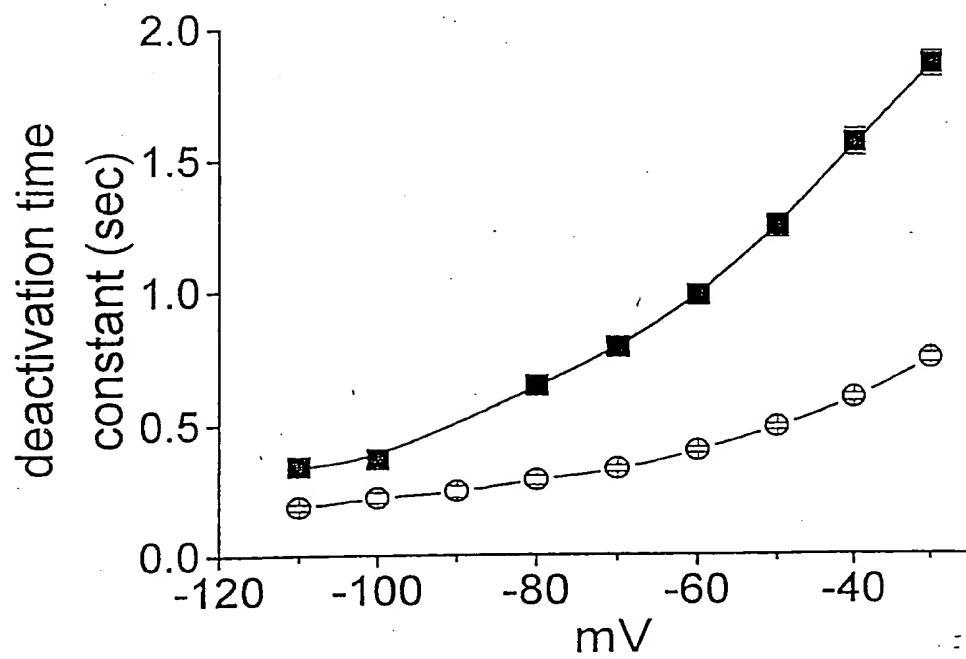


Figure 16D

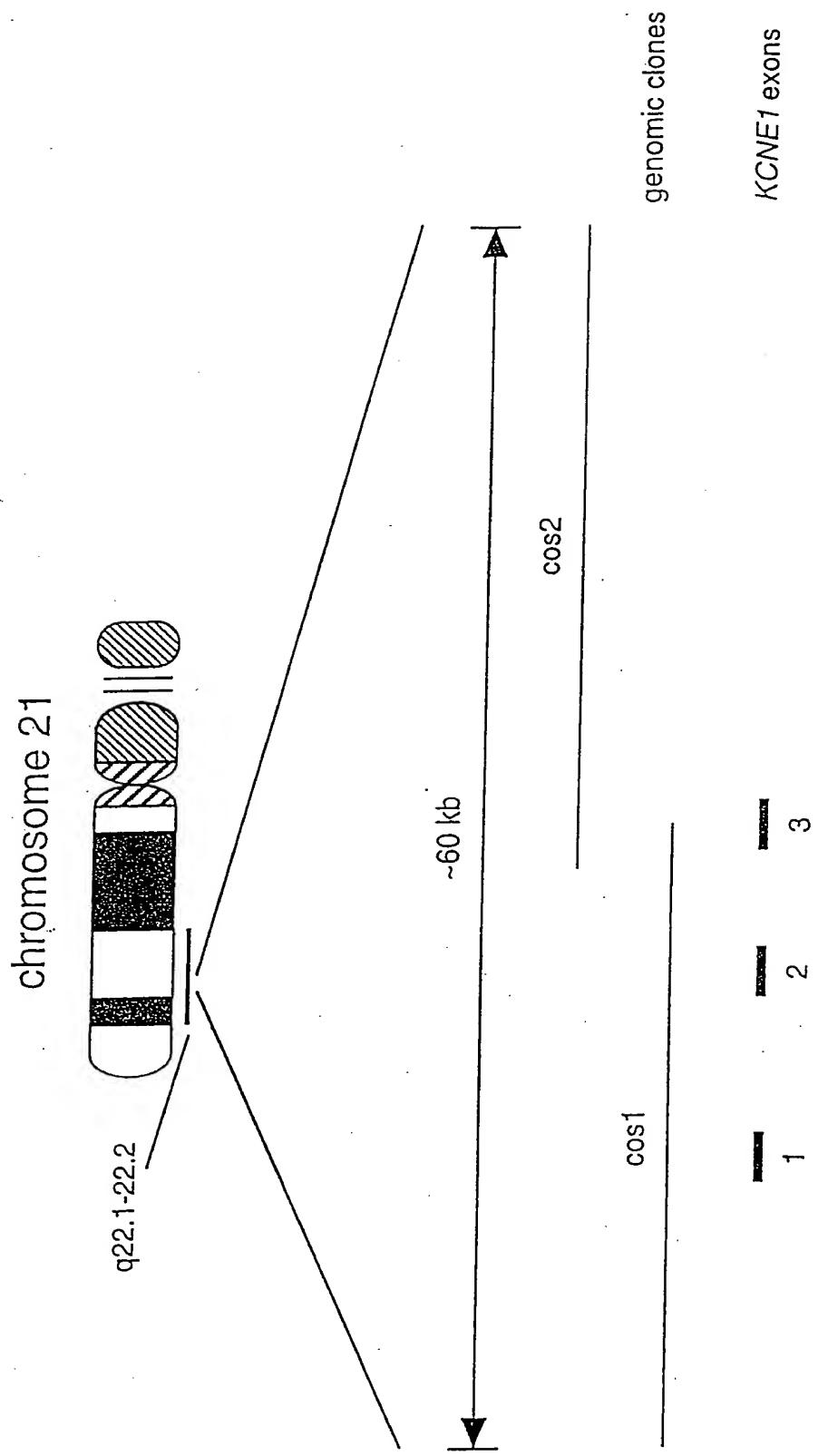


Figure 17

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 M I L S N T T A V T P F L T K L W -17  
 CAGGAGACAGTCAGCAGGGTGGCAACATGTCGGGCTGGCCGCAGGTCCCCCGCAGCGGTGACGCCAGCTGGAGGCC-324  
 Q E T V Q Q G G N M S G L A R R S P R S G D G K L E A -44  
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 L Y V L M V L G F F G E F T L G I M L S X I R S K K L -71  
 GAGCACTCGAACGCCATTCAACGTCATCGAGTCCGATGCCCTGGCAAGAGAAGGGACAAGGCCATGTCAGGCCGG-486  
 E H S N D P F N V Y I E S D A W Q E K D K A Y V Q A R -98  
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 V L E S Y R S C Y V V E N H L A I E Q P N T H L P E T -125  
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 TACTCTTATTGTGATGGATACCACTGGATTCTTTGGCTGTTGTAANGGTGAGGGGTGGATTAATGACACTGTTCA-729  
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 TCTTCCCTTAAGCCAATGTTATTCTGATCTCTGTTAAGGTGCGAGAATCAATGCCCTTACTGATAACACCTACCTTATAGGAC-1215  
 TGAACCTAAAGGCATGACATTTCATACTTGTCAAGCACACTGATTCTCCCTTGTCACTTCTGTGCTCACTTTGT-1296  
 GGCTCTATCCTCCCTGCCCTCCGCTTCCACTCCTCCCTGACCCATCCTGCACACATCTCCCTGAAAACACACAGG-1377  
 CACATACACTCATACATAGACACACATACACACCTCAATCTAGAAAGAAACTTGCTTGTACAGGGCTGAGATGGAGGAG-1458  
 AAAAAATGCCCTTCAGAATGCATACCAAGGGAGGTGCTGGTCACTGTGGAGCAGGGAAAGGTGCCCTTCACTCCC-1539  
 CGAGAGCCAGGGAGGTGGCTCTGGCAGAGAGGGACACATAGCACTGGGTGGCAGGTCTTTGAGGTGATGGGCC-1620  
 GGTGAGATGAATTGTATCCCCAAAAAGACAGGTACCTCAATGTGACCTAATTGGAAATAGAGTCTTGAGAT-1701  
 G(A)n -1702

Figure 18